The Relation of Occupational Organic Solvent Exposure to Symptom Reporting in a Sample of White and Chinese Midlife Women

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Objective: *This study examined the relation of occupational solvent exposure to menopausal and other symptoms in midlife women.* ***Methods:*** *We conducted a cross-sectional study of 480 Chinese and 494 white women, aged 40–55 years, in Northern California. Levels of exposure to organic solvents (none, low, medium, or high) were assigned to each current job using a job-exposure matrix.* ***Results:*** *A lower proportion of women with low occupational organic solvent exposure reported hot flashes or night sweats than working women with no solvent exposure (adjusted prevalence odds ratio [APOR] = 0.48, 95% confidence interval [CI] = 0.19–1.21). A greater proportion of women with high solvent exposure reported forgetfulness than women with no exposure (APOR = 2.51, 95% CI = 1.12–5.63).* ***Conclusions:*** *Some symptom reporting in midlife women was related to their occupational organic solvent exposure.* (J Occup Environ Med. *2005;47: 410–423*)

Several studies have examined the effect of occupational organic solvent exposure on reproductive function in women. All but one of these studies have focused on adverse pregnancy outcomes and hazards to fertility, including abnormalities of menstrual function.[1] Almost no information exists about how these chemicals affect ovarian function and physical and psychologic symptoms in midlife women.

A Polish study found that women exposed to carbon disulfide in a synthetic fibers factory were twice as likely to be postmenopausal as a control group of similarly aged women working in a clothing factory with no exposure to carbon disulfide.[2,3] Furthermore, the mean age at menopause in exposed women was 43.9 years compared with 48.1 years in the control group. An effect on ovarian function was also evidenced in the lower serum concentrations of estrone, estradiol, and progesterone in the women chronically exposed to carbon disulfide compared with the control women. A recent study of female U.S. Air Force employees with fuel and solvent exposure found that preovulatory luteinizing hormone (LH) levels were significantly lower in women whose total aliphatic hydrocarbon levels measured in exhaled breath were above the median.[4] Based on the findings of these and other studies that have shown an increased risk of irregular cycles,[5] dysmenorrhea (painful menses),[6] and oligomenorrhea (long cycle length)[7] among workers exposed

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to organic solvents, vasomotor symptoms may plausibly be associated with organic solvent exposures in working women during the years of menopausal transition.

Organic solvents also affect the central nervous system, and workplace exposure has been associated with both physical and psychologic symptoms such as headaches, fatigue, irritability, difficulty concentrating, and memory loss.[8–14] In the Polish study, more women exposed to carbon disulfide reported headaches than women in the control group.[2,3] The purpose of the present study was to examine the relation of occupational organic solvent exposure to 12 self-reported physical and psychologic symptoms in midlife white and Chinese women while controlling for menopausal status and several important demographic, lifestyle, and health variables.

Subjects and Methods

Study Population

Women were recruited for the Study of Women's Health Across the Nation (SWAN), a multiethnic community-based study of the health of middle-aged women, conducted at seven sites across the United States.[15] The present analysis is based on data that was only collected at the Northern California site. These data were obtained during the screening phase for SWAN, consisting of a cross-sectional telephone survey conducted from 1995 through 1997, which determined eligibility of women for enrollment into a longitudinal study of pre- and early perimenopausal women and investigated cross-sectional relations of a number of risk factors and health outcomes.

The sampling frame for the Northern California site consisted of all white and Chinese women aged 40–55 years who were members in 1995 of the Kaiser Permanente Medical Care Program and resided in Oakland, Hayward, or Richmond, California. Because race/ethnicity was not explicitly stated in Kaiser's computerized records, patients' names[16] were used to form the race/ethnic strata from which to sample. Women were selected from each stratum in batches of 200 using simple random sampling. Batches were selected until the target sample size of eligible, willing-to-participate women (250 Chinese and 200 white) for the longitudinal follow-up portion of the study was attained. Fifteen attempts were made to contact and interview each woman in a batch before women in the next batch were contacted. A total of 1897 non-Chinese surnamed women and 1400 women with a Chinese first or last name were sent letters inviting them to participate in the study. The study was approved by the Institutional Review Boards at the University of California Davis and Kaiser Permanente. Verbal consent for the screening interview was obtained by telephone before administration of the survey.

Eligibility for the cross-sectional study was determined through a brief set of questions that immediately preceded the full 15-minute interview. To be eligible, a woman had to: be 40–55 years old at initial contact; identify her race/ethnic group as white, Chinese, or Chinese American; speak English or Cantonese; and reside in the study area. Once a woman was determined to be eligible, she was asked to identify her primary race/ethnic group, which did not always match her surname group. The participation rates were 80.9% for the non-Chinese and 72.1% for the Chinese women. The refusal rates were 9.4% and 17.8%, respectively, and the remaining nonparticipants had moved out of the area, were untraceable, had died, or did not answer after 15 telephone calls. We have no information about the significantly higher refusal rate among the Chinese women. A total of 1516 (59.6%) women at the Northern California site were eligible and completed the telephone cross-sectional interview.

Data Collection

The cross-sectional interview contained questions on health, reproductive history, symptoms, lifestyle factors (such as smoking and physical activity), disability, social support, and demographic factors. All questions were translated into Cantonese and independently backtranslated, and any discrepancies were resolved by the two translators.

Dependent Variables. Women were asked to respond to a "yes/no" question regarding the presence or absence in the past 2 weeks of the following symptoms: hot flashes; night sweats; leaking urine; vaginal dryness; difficulty sleeping; headaches; heart pounding or racing; stiffness or soreness in joints, neck, or shoulders; forgetfulness; feeling tense or nervous; feeling blue or depressed; irritability or grouchiness. The selection of these symptoms was based primarily on previous epidemiologic studies of white women,[17–20] although many of these symptoms have also been reported recently in Chinese women.[21–23] Symptoms reported in the anthropologic literature[24] and in focus groups conducted with all of the ethnic groups before initiation of the cross-sectional survey[25] were also included. In addition to symptoms, a question about general health was included: "Would you say your health in general is excellent, very good, good, fair, or poor?"

Exposure Assessment. The SWAN cross-sectional survey contained a question from the U.S. Census, which asked whether the woman had worked at a job for pay or had performed unpaid work in the family farm or business during the past 2 weeks. At the Northern California site, we added questions about job title, usual job activities, and industry of employment. Each woman could report up to three jobs held during the past 2 weeks. Trained[26] coders assigned four-digit codes for occupation and for industry using the 1980 *Standard Occupational Classi-*

fication Manual (SOC)[27] and the 1987 *Standard Industrial Classification Manual* (SIC).[28] Two people coded each job, and a third trained person (RG) made the final coding decision for any discrepancies between coders.

Exposure to organic solvents was assigned to each job by linking these codes to a job-exposure matrix developed by industrial hygienists at the National Cancer Institute.[29,30] The category of organic solvents included both aromatics (benzene, xylene, toluene, and so on) and aliphatics (trichloroethylene [TCE], perchlorethylene [PERC], carbon tetrachloride, and so on). The assignment of exposure was based on data from the literature, unpublished industrial hygiene reports and inspections, and personal judgment of the project industrial hygienists.

Each industry and occupation was assigned a semiquantitative estimate (none, low, medium, high) of probability and of intensity of exposure to any organic solvent. Probability was conceptualized as the likelihood that any organic solvent was used by a worker in that industry or occupation. Intensity was based on expected level of exposure and frequency of use. Estimates of probability and intensity of exposure were assigned to each industry–occupation combination through the use of an algorithm,[31] which used either occupation alone or both occupation and industry, depending on the specificity of the exposure environment that could be inferred from the occupational (SOC) code. For example, a printer would be assigned the same probability and intensity level of exposure to organic solvents irrespective of the industry in which she was employed. In contrast, for managers and assemblers, assignments of probability and intensity depended on both occupation and industry. If a woman reported more than one job held in the past 2 weeks, exposure to organic solvents was assigned by taking the mean of the intensity scores and the mean of the probability scores of all her current jobs. Only 7% of working women reported more than one current job. All intensity and probability assignments were made without knowledge of outcome (symptoms).

Covariates. The cross-sectional survey contained standardized questions about several important covariates, which have been associated with symptoms in previous literature,[18–20,22,32–35] including age; smoking (never, past, current); educational level; race/ethnicity; preferred language; amount of physical activity compared with other women of the same age; body mass index (BMI) computed as weight in kilograms divided by the square of height in meters; parity; marital status; ability to pay for basics; and menopausal status. As a result of the need for a short screening survey, data were not collected regarding prior neurologic or psychiatric illness or medications used.

Data Analyses

Exclusions. We excluded 77 women at this site because they reported their primary race/ethnicity to be other than white or Chinese and 15 women whose menstrual periods had stopped as a result of medication, radiotherapy, pregnancy or lactation, or extreme weight change. An additional 340 women who reported exogenous female hormone use in the past 3 months were excluded because hormone use could obscure bleeding patterns making it difficult to assess menopausal status accurately in these women and could affect symptom reporting. We further excluded 110 women because occupational information was missing and 123 because they were not working, leaving a total for the present analyses of 415 Chinese and 436 white women.

Outcome Data. To determine whether we could combine some symptoms in the analysis, we examined patterns of symptom reporting using the SAS version 6 PROC FREQ procedure with the LIST option.[36,37] The only consistent pattern was that vasomotor symptoms (hot flashes and night sweats) tended to occur together, similar to the findings of Avis et al.[32]

Exposure Data. We performed separate logistic regression analyses for intensity and for probability of organic solvent exposure. In each analysis, we combined women with medium and high exposure levels, because too few women had high-intensity or probability of exposure to form a separate group. We also created a third exposure variable, which grouped women with respect to intensity and probability of occupational organic solvent exposure and classified individuals into one of four categories, women with: 1) zero probability of exposure, 2) low-intensity and low probability of exposure, 3) low-intensity and medium or high probability, and 4) medium- or high-intensity and medium or high probability of exposure. We excluded from the models the three women with medium- or high-intensity and low probability of exposure, because this was not a large enough number of women to form a separate category.

Multivariate Analyses. Initially, we selected potentially confounding variables that had been shown in the literature to be associated with either symptoms or occupation. We then performed chi-squared analyses of each of these variables by each symptom and by probability and intensity of occupational exposure to organic solvents. We also assessed the relationship between hot flashes or night sweats and difficulty sleeping, because the vasomotor symptoms may adversely affect sleep. For each symptom, a variable was considered for inclusion in a multiple logistic model if the *P* values for the chi-squared associations between that variable and the symptom and the same variable and intensity or probability of organic solvent exposure were both less than 0.20. Thus, the following variables were selected for initial inclusion into at least one

multiple logistic model of the relationship between a symptom and occupational exposure to organic solvents: occupational status, age, smoking, educational level, ability to pay for basics, menopausal status, race/ethnicity/language (Cantonese or English), physical activity, BMI, parity,[35] history of arthritis, level of reported disability, marital status, availability of help with daily chores or someone to talk with, and number of close friends or relatives. Menopausal status was defined as follows: surgical, postmenopausal (at least 12 months of amenorrhea), late perimenopausal (having a period in the last 3–11 months), early perimenopausal (having a period in the last 3 months but reporting more irregularity), or premenopausal (having a period in the last 3 months and not reporting increased irregularity). Too few women reported a history of heart attack or angina ($n = 6$) to include this variable in the model for the symptom "heart pounding."

We performed separate unconditional multiple logistic regression analyses for each symptom or symptom combination. For each logistic regression model, we initially included dummy variables representing the categories of organic solvent exposure and all covariates that were associated with organic solvent exposure and the symptom in the two-way analyses. To arrive at a final model, we performed a best subsets logistic regression using the "selection = score" option in SAS's PROC LOGISTIC.[36,37] We used the difference in the score statistics between models to determine the final model and selected the model that included the fewest covariates without a significant change in the score statistic from the previous model while including all logical categories of covariates. For each final model, we performed a Hosmer and Lemeshow goodness-of-fit test.[38] We also included an interaction term for race/ethnicity by organic solvent exposure into each model to determine if it significantly improved the fit of the model.

Results

Characteristics by Race/Ethnicity

The white and Chinese women differed with respect to several characteristics. Compared with the white women, the Chinese women were younger, much less likely to have ever smoked, less likely to have had a surgical menopause, more likely to be premenopausal, more likely to have had less than 12 years of education, more likely to be married, less likely to report a physical disability, and had lower BMI, higher parity, less help with daily chores, and fewer close friends or relatives.

Jobs Associated With Exposures and Outcomes

The low intensity, low probability of exposure category was comprised largely of healthcare workers, particularly registered nurses (Table 1). The most frequent job titles in the low-intensity, medium or high probability of exposure were clinical laboratory technologists and technicians, maids and housemen, and janitors and cleaners. Hairdressers and cosmetologists, assemblers, precision electrical equipment assemblers, and laundering and dry cleaning machine operators were the most frequently reported job titles in the medium–high-intensity category. Among working women with no exposure to organic solvents, the most frequent job titles were bookkeepers, secretaries, elementary school teachers, accountants, managers: administrative services, and textile sewing machine operators.

Among workers in the low-intensity, low-probability category, the prevalence of hot flashes was 0% in registered nurses, physicians, and pharmacists ($n = 29$) but 23.1% in nursing and other health aides ($n = 13$) (Table 2). In the medium- or high-intensity category, hairdressers and cosmetologists had a prevalence of 16.7% for hot flashes and 25.0% for night sweats. The prevalence of headache was lower among the registered nurses, physicians, and pharmacists than among bookkeepers and secretaries, and teachers (20.7% vs. 51.6% and 47.8%), but nursing and other health aides had a prevalence of headache of 53.9%, which was similar to the bookkeepers and teachers. The nursing and other health aides reported the highest prevalence of stiffness (69.2%) among the selected job titles reported in Table 1. Because similar numbers of white and Chinese women were working in these job categories, the prevalence rates were not strongly confounded by race/ethnicity.

Characteristics by Occupational Exposure to Organic Solvents

Most of the covariates that were initially included in the multiple logistic regression models were strongly associated with organic solvent exposure (Table 3) in the two-way analyses ($P < 0.05$). Although age was not associated with organic solvent exposure, it was initially included in all the logistic regression models in which it was associated with the outcome in the bivariate analyses. Chinese women were more likely to have jobs with organic solvent exposure, particularly jobs with medium or high intensity or probability of exposure, and were less likely to report most symptoms (Table 4) than white women. Compared with women in jobs with no or low-intensity exposure, women in medium- or high-exposure jobs were more likely to be current smokers, to have difficulty paying for basics, and to have low job status. They were also less likely to be premenopausal, to have a college education, or to have help with daily chores.

TABLE 1
Job Titles by Solvent Exposure for all Jobs* Reported by Working Chinese and White Midlife Women

Organic Solvent Exposure Category	Job Title	No.	Percent of Total Jobs Reported
No exposure†	Bookkeepers and accounting and auditing clerks	33	3.5
	Secretaries	32	3.4
	Elementary school teachers	30	3.2
	Accountants and auditors	24	2.6
	Managers: administrative services	24	2.6
	Textile sewing machine operators and tenders	24	2.6
	Management-related occupations, not elsewhere classified	19	2.0
	Managers; medicine and health	18	1.9
	Secondary school teachers	18	1.9
	Adult education and other teachers, not elsewhere classified	17	1.8
	Computer systems analysts	15	1.6
	Prekindergarten and kindergarten teachers	15	1.6
	Social workers	15	1.6
	Cashiers	13	1.4
	General office occupations	12	1.3
	Postal clerks, except mail carriers	12	1.3
	Financial managers	10	1.1
	Investigators and adjusters, except insurance	10	1.1
	Psychologists	10	1.1
	Managers; food serving and lodging establishments	9	1.0
Low-intensity, low probability of exposure	Registered nurses	25	2.7
	Licensed practical nurses	4	0.4
	Health technologists and technicians, not elsewhere classified	3	0.3
	Nursing aides, orderlies, and attendants	3	0.3
	Pharmacists	3	0.3
	Physicians	3	0.3
	Health aides, except nursing	2	0.2
	Supervisors; precision production occupations	2	0.2
	Animal caretakers, except farm	1	0.1
	Art, drama, and music teachers	1	0.1
	Biologic scientists	1	0.1
	Civil engineers	1	0.1
	Dental assistants	1	0.1
Low-intensity, medium–high probability of exposure	Clinical laboratory technologists and technicians	10	1.1
	Maids and housemen	10	1.1
	Janitors and cleaners	7	0.8
	Mail carriers, post office	4	0.4
	Photographic processing machine operators	2	0.2
	Dental hygienists	1	0.1
	Electricians	1	0.1
	Engineers, not elsewhere classified	1	0.1
	Managers, horticultural specialty farms	1	0.1
	Medical scientists	1	0.1
	Purchasing agents and buyers, not elsewhere classified	1	0.1
	Purchasing managers	1	0.1
	Samplers	1	0.1
	Stock and inventory clerks	1	0.1
	Supervisors; production occupations	1	0.1
	Traffic, shipping, and receiving clerks	1	0.1

TABLE 1
Job Titles by Solvent Exposure for all Jobs* Reported by Working Chinese and White Midlife Women (continued)

Organic Solvent Exposure Category	Job Title	No.	Percent of Total Jobs Reported
Medium–high-intensity, low–high probability of exposure	Hairdressers and cosmetologists	12	1.3
	Assemblers	5	0.5
	Precision electrical and electronic equipment assembler	5	0.5
	Laundering and dry cleaning machine operators‡	4	0.4
	Chemists, except biochemists‡	2	0.2
	Painters, sculptors, craft artists and artist–printmakers	2	0.2
	Printing machine operators and tenders	2	0.2
	Science technologists and technicians, not elsewhere classified	2	0.2
	Fabricators, not elsewhere classified	1	0.1
	Hand molding and casting occupations	1	0.1
	Hand packers and packagers	1	0.1
	Machinists	1	0.1
	Miscellaneous machine operators and tenders, not elsewhere classified	1	0.1
	Nursery workers	1	0.1
	Photoengraving and lithographing machine setup operators	1	0.1
	Plating and coating machine operators and tenders	1	0.1
	Precision hand molders and shapers (jewelers)	1	0.1
	Pressing machine operators	1	0.1
	Supervisors; production occupations	1	0.1
	Water and sewage treatment plant operators	1	0.1

*A total of 930 jobs were held by 851 working women. Some women reported two or three jobs held concurrently.
†The 20 most frequently reported jobs in this category.
‡One laundering and dry cleaning machine operator (pressing industry) and two chemists were excluded from the final analyses because they were in the low-probability category.

Prevalence of Symptoms and Health Status in Relation to Occupational Exposure to Organic Solvents and Race/Ethnicity

Few clear trends of increasing or decreasing symptom reporting with increasing exposure to organic solvents were observed in the unadjusted analyses (Table 4). Among both Chinese and white women, the prevalence of hot flashes was much lower in women with low-intensity, low-probability exposure jobs than in any other category, including working women with no exposure. The prevalence of headache was lowest among women in the two low-intensity categories, whereas the prevalence of forgetfulness was highest among women in the highest exposure category. Only 33.4% of white and 22.7% of Chinese women in the highest exposure category reported good or excellent health, compared with 82.6% of white and 55.5% of Chinese women in the low-intensity, low-probability exposure group.

Adjusted Associations of Symptoms and Health Status With Occupational Exposure to Organic Solvents

After adjusting for potential confounders, women with low intensity and low probability of exposure to organic solvents had a lower prevalence of hot flashes or night sweats than working women with no solvent exposure (adjusted prevalence odds ratio [APOR] = 0.48, 95% confidence interval [CI] = 0.19–1.21) (Table 5). No clear trend in prevalence of urine leakage was observed by exposure categories, and no exposure group appeared to have elevated prevalence. Among working women, the APOR for difficulty sleeping increased with increasing intensity and probability of exposure. Women in the two low-intensity categories had a much lower prevalence of headache (APOR = 0.51 and 0.40, respectively; 95% CI = 0.27–0.98 and 0.18–0.87) than unexposed working women.

Women in the highest exposure category were significantly more likely to report forgetfulness than working women with no exposure (APOR = 2.51, 95% CI = 1.12–5.63), whereas women in the low-intensity, low-probability category were less likely to report the same symptom (APOR = 0.57, 95% CI = 0.28–1.16). Women in the three solvent-exposed categories were less likely than working women with no solvent exposure to report feeling tense or nervous with APORs ranging from 0.52 to 0.64. The prevalence of reporting feeling blue or depressed was similar in all groups, except that women in the low-intensity, medium–high-probability

TABLE 2
Unadjusted Prevalence (percent) of Self-Reported Symptoms and General Health by Selected Job Titles and Their Probability and Intensity of Occupational Exposure to Organic Solvents Categories in Middle-Aged Working Chinese and White Women

	Occupational Exposure to Organic Solvents						
	No Exposure		Low Intensity, Low Probability		Low Intensity, Medium Probability		Medium intensity, medium probability
Symptoms	Bookkeepers, secretaries	Elementary, secondary school teachers	Nursing aides, other health aides*	Registered nurses, physicians, pharmacists	Janitors, maids	Clinical laboratory technicians	Hairdressers and cosmetologists
	(*N* = 64)	(*N* = 47)	(*N* = 13)	(*N* = 29)	(*N* = 17)	(*N* = 11)	(*N* = 12)
Hot flashes	14.1	26.1	23.1	0.0	5.9	18.2	16.7
Night sweats	12.7	23.9	23.1	3.5	11.8	0.0	25.0
Urine leakage	15.6	13.0	23.1	13.8	11.8	9.1	16.7
Vaginal dryness	14.1	8.7	16.7	10.3	11.8	9.1	0.0
Difficulty sleeping	42.2	37.0	61.5	20.7	11.8	45.5	50.0
Stiffness/soreness	56.3	45.7	69.2	37.9	35.3	27.3	33.3
Headache	51.6	47.8	53.9	20.7	17.7	45.5	16.7
Heart pounding	18.8	13.0	7.7	6.9	23.5	18.2	8.3
Forgetfulness	43.8	32.6	53.9	13.8	41.2	18.2	25.0
Tense/nervous	45.3	60.9	53.9	44.8	35.3	36.4	41.7
Depression	42.2	32.6	46.2	31.0	23.5	18.2	16.7
Irritability	53.1	58.7	53.9	48.3	41.2	54.6	41.7
General health							
Excellent	23.4	34.8	23.1	44.8	0.0	9.1	33.3
Very good	35.9	37.0	30.8	34.5	17.7	54.6	16.7
Good	28.1	28.3	38.5	17.2	29.4	36.4	25.0
Fair	12.5	0.0	7.7	3.5	52.9	0.0	25.0
Poor	0.0	0.0	0.0	0.0	0.0	0.0	0.0

*Includes licensed practical nurses, health technicians, and dental assistants.

exposure group were significantly less likely to report this symptom (APOR = 0.36, 95% CI = 0.14–0.89). After adjusting for several confounding demographic and lifestyle variables, women with low intensity, low probability of exposure jobs reported the best general health of all groups of women. The APOR for good or very good versus excellent health was 0.44 (95% CI = 0.22–0.89) for working women in this lowest exposure group compared with working women with no exposure to organic solvents.

The remaining symptoms did not appear to be related to organic solvent exposure among working women. In addition, no evidence of an interaction between occupational organic solvent exposure and race/ethnicity for any of the symptoms or symptom groups was observed, although race/ethnicity or language of the interview was related to symptom reporting in the final logistic regression models for all symptoms.

Discussion

In the present study, women working in jobs with medium or high intensity of exposure to organic solvents were more than twice as likely to report forgetfulness as working women with no exposure. This group of women was also more likely to report fair or poor health compared with other working women. Women in jobs with low-intensity exposure actually were less likely than other working women to report some symptoms, including hot flashes or night sweats (vasomotor symptoms), headache, and feeling blue or depressed.

Vasomotor Symptoms

The group of women working in jobs with low-intensity exposure to organic solvents was largely comprised of health professionals such as nurses, physicians, and clinical laboratory technicians. The lower prevalence of hot flashes or night sweats in this group may have been the result of selection bias attributed to the higher percentage of these women using hormone replacement therapy (HRT). We excluded women using HRT in this analysis because previous studies[33,39,40] have indicated that women who are taking HRT may actually have more symptoms than women not on hormones, either because of a failure of hormones to mitigate symptoms or a higher baseline level of symptoms among HRT users. Before this exclusion, 36.7% of the women in the low-intensity, low probability of exposure group reported taking hormones in the past 3 months versus only 13.0% of women in the medi-

TABLE 3
Distribution of Study Population by Occupational Exposure to Organic Solvents and Selected Characteristics

Characteristic	Total	Intensity and probability of occupational exposure to organic solvents: None		Low intensity, low probability		Low intensity, medium or high probability		Medium to high intensity, med or high probability		
	Percent	No.	Percent	No.	Percent	No.	Percent	No.	Percent	*P* value
Total	100.0	717	100.0	50	100.0	41	100.0	40	100.0	
Ethnicity/language										
White	51.3	386	53.8	23	46.0	8	19.5	18	45.0	<0.001†
English-speaking Chinese	25.0	176	24.6	20	40.0	12	29.3	4	10.0	
Cantonese-speaking Chinese	23.7	155	21.6	7	14.0	21	51.2	18	45.0	
Age (yr)										
40–43	32.2	224	31.2	19	38.0	16	39.0	14	35.0	0.874†
44–47	34.4	251	35.0	17	34.0	10	24.4	14	35.0	
48–51	22.6	164	22.9	8	16.0	11	26.8	9	22.5	
52–55	10.7	78	10.9	6	12.0	4	9.8	3	7.5	
Smoking‡										
Never smoked	70.3	478	70.4	35	71.4	34	87.2	15	46.9	0.004§
Past smoker	19.7	136	20.0	11	22.5	2	5.1	8	25.0	
Current smoker	10.0	65	9.6	3	6.1	3	7.7	9	28.1	
BMI (weight [kg]/height [m^2])										
<27	77.6	548	76.8	41	82.0	37	90.2	30	75.0	0.305§
27–31.9	12.9	95	13.3	5	10.0	4	9.8	5	12.5	
32+	9.5	71	9.9	4	8.0	0	0.0	5	12.5	
Menopausal status										
Surgical or postmenopausal	15.5	113	15.9	5	10.2	8	19.5	4	10.2	0.010†
Perimenopausal	38.5	285	40.1	10	20.4	10	24.4	18	46.2	
Premenopausal	46.0	312	43.9	34	69.4	23	56.1	17	43.6	
Education										
<12 yr	9.1	58	8.1	2	4.0	9	22.0	8	20.0	<0.001†
High school graduate or GED	16.8	113	15.8	2	4.0	10	24.4	17	42.5	
Some college or vocational school	26.0	186	26.0	15	30.0	11	26.8	8	20.0	
College graduate	23.4	171	23.9	17	34.0	7	17.1	3	7.5	
Graduate or professional school	24.8	188	26.3	14	28.0	4	9.8	4	10.0	
Difficulty paying for basics										
Very	5.9	38	5.3	3	6.0	2	4.9	7	17.5	0.002§
Somewhat	26.4	188	26.4	7	14.0	11	26.8	17	42.5	
Not at all	67.7	487	68.3	40	80.0	28	68.3	16	40.0	
Marital status										
Never married	9.1	66	9.2	5	10.0	3	7.3	3	7.5	0.427§
Married, living as married	73.6	517	72.2	38	76.0	35	85.4	33	82.5	
Separated, divorced, widowed	17.3	133	18.6	7	14.0	3	7.3	4	10.0	
Physical activity level compared with women the same age										
Less	18.4	134	19.9	5	10.2	2	5.1	5	16.1	0.145†
About the same	41.1	275	40.8	23	46.9	18	46.2	10	32.3	
More	40.5	265	39.3	21	42.9	19	48.7	16	51.6	
Parity										
0	19.6	147	20.5	8	16.0	4	9.8	7	17.5	0.153†
1	18.9	137	19.1	11	22.0	4	9.8	8	20.0	
2	40.1	277	38.7	18	36.0	25	61.0	20	50.0	
3	15.8	111	15.5	12	24.0	7	17.1	4	10.0	
4+	5.6	44	6.2	1	2.0	1	2.4	1	2.5	
Level of disability										
No disability	81.2	577	80.6	42	84.0	38	95.0	30	75.0	0.059§
Some disability	16.0	119	16.6	8	16.0	2	5.0	6	15.0	
Quite limited	2.8	20	2.8	0	0.0	0	0.0	4	10.0	
Availability of help with daily chores or someone to talk with										
None to some of the time	36.9	255	35.9	13	26.0	22	53.7	21	52.5	0.030†
Most of the time	38.9	282	39.7	25	50.0	11	26.8	9	22.5	
All of the time	24.2	174	24.5	12	24.0	8	19.5	10	25.0	

TABLE 3
(Cont'd)

Number of close friends or relatives										
0	2.4	15	2.1	1	2.0	1	2.4	3	7.5	0.314†
1–2	16.2	113	15.8	9	18.0	9	22.0	6	15.0	
3–4	26.1	193	27.0	10	20.0	11	26.8	7	17.5	
5–9	33.9	234	32.7	22	44.0	16	39.0	15	37.5	
10 or more	21.5	161	22.5	8	16.0	4	9.8	9	22.5	
Occupational status score										
1–44	25.0	155	21.6	6	12.0	21	51.2	30	75.0	<0.001†
45–70	25.4	195	27.2	10	20.0	2	4.9	8	20.0	
71–85	25.4	173	24.1	25	50.0	15	36.6	2	5.0	
86–99	24.3	194	27.1	9	18.0	3	7.3	0	0.0	

*Categories may not always sum to total as a result of missing values.
†*P* value from Pearson chi-square.
‡Missing values as a result of problems with initial translation into Cantonese.
§*P* value from Fisher exact test.

um–high-intensity, medium–high-probability group and 24.3% of working women with no solvent exposure. Thus, women in the low-intensity, low probability of exposure group were disproportionately excluded from the analyses. In the group of HRT users excluded from this analysis, the prevalence of hot flashes was actually higher in the low-intensity, low-probability group ($n = 29$) than in the working women with no solvent exposure (34.5% vs. 22.1%), although the numbers were small. Thus, those excluded had a higher prevalence of hot flashes, leaving a lower prevalence of hot flashes in the low-exposure group after HRT users were excluded. The prevalence of night sweats was about the same in HRT users and nonusers.

Although the prevalence of vasomotor symptoms was moderately elevated among women with medium–high intensity and medium–high probability of exposure compared with working women with no exposure (APOR = 1.27), women in the exposed group were less likely to use HRT than nonexposed women. Therefore, selection bias may also have played a role in that modest increase. However, the six women with medium–high-intensity exposure who were taking HRT had the highest prevalence of hot flashes and night sweats. A larger sample of women would be necessary to draw any conclusions about highly exposed women who take HRT.

The only previous study of which we are aware that examined the relationship between menopausal symptoms and occupational organic solvent exposure was conducted with women in Poland who were chronically exposed to carbon disulfide at a synthetic fibers factory.[2,3] A comparison group of unexposed workers was selected from a clothing factory without exposure to carbon disulfide but with similar occupational conditions. The authors based their investigation on women from each group who had symptoms of menopause or who were postmenopausal. They reported that the women in the control group were more likely to report hot flashes than the women in the exposed group. However, the average age at menopause was much lower in the exposed women (43.9 years) compared with the controls (48.1 year). Therefore, the exposed women may have been less likely to report hot flashes because more years had elapsed since their last menstrual period, although such information was not provided. Although the serum concentrations of estrone, estradiol, and progesterone were significantly decreased in women chronically exposed to carbon disulfide, no significant differences in the level of follicle-stimulating hormone or luteinizing hormone were noted between the two groups.

Although the Polish study is the only one to date that has examined the effect of organic solvent exposure on menopausal symptoms, several studies have examined the relationship between occupational organic solvent exposure and menstrual disorders. Such studies are relevant because organic solvents may affect menstrual function by influencing the hormonal balance regulated by the hypothalamus–pituitary–ovarian axis, which could also affect menopausal symptoms.[1] Gold et al[5] found that women in the semiconductor industry working in photolithography, in which several organic solvents were used, reported significantly more variability in menstrual cycle length than nonfabrication workers. Blatter and Zielhuis[41] found that, compared with shop assistants, hairdressers were more likely to experience amenorrhea, irregular cycles, oligomenorrhea (long cycle length), long blood loss, and dysmenorrhea. Dysmenorrhea was also reported more frequently in factory workers exposed to toluene[42] and dry cleaning workers exposed to perchlorethylene.[43] In a study of menstrual disorders among military personnel, Gordley et al[6] found that twice as many women who reported handling jet fuel reported dysmenorrhea as women having no fuel contact. The jet fuel consisted of al-

TABLE 4
Unadjusted Prevalence (percent) of Self-Reported Symptoms and General Health by Probability and Intensity of Occupational Exposure to Organic Solvents Categories in Middle-Aged Chinese and White Women

	Non-Hispanic White				Chinese			
	Probability and Intensity of Occupational Exposure to Organic Solvents				Probability and Intensity of Occupational Exposure to Organic Solvents			
Symptoms	None	Low Intensity, Low Probability	Low Intensity, Medium or High Probability	Medium to High Intensity, Medium or High Probability	None	Low Intensity, Low Probability	Low Intensity, Medium or High Probability	Medium to High Intensity, Medium or High Probability
	(*N* = 386)	(*N* = 23)	(*N* = 8)	(*N* = 18)	(*N* = 331)	(*N* = 27)	(*N* = 33)	(*N* = 22)
Hot flashes	22.7	8.7	25.0	16.7	15.9	3.9	9.1	9.1
Night sweats	21.7	13.1	12.5	33.3	12.4	7.4	9.1	9.1
Urine leakage	19.8	21.7	25.0	27.8	10.6	14.8	6.1	13.6
Vaginal dryness	12.6	9.1	37.5	16.7	11.3	11.1	3.0	4.8
Difficulty sleeping	45.5	39.1	37.5	55.6	31.1	33.3	30.3	36.4
Stiffness/soreness	57.4	43.5	50.0	72.2	52.0	48.2	33.3	54.6
Headache	52.2	26.1	25.0	33.3	40.9	33.3	24.2	36.4
Heart pounding	16.9	13.0	0.0	22.2	14.2	3.7	18.2	4.6
Forgetfulness	35.3	21.7	25.0	55.6	43.2	25.9	36.4	59.1
Tense/nervous	62.9	65.2	25.0	61.1	44.7	25.9	36.4	22.7
Depression	44.4	43.5	0.0	33.3	34.1	25.9	21.2	31.8
Irritability	57.1	56.5	25.0	66.7	46.8	37.0	45.5	45.5
General health								
Excellent	25.5	47.8	25.0	16.7	15.7	29.6	9.1	0.0
Very good	42.6	34.8	37.5	16.7	29.3	25.9	33.3	22.7
Good	26.2	13.0	37.5	50.0	32.9	37.0	30.3	36.4
Fair	4.7	4.4	0.0	11.1	19.9	7.4	27.3	36.4
Poor	1.0	0.0	0.0	5.6	2.1	0.0	0.0	4.6

kanes, cycloalkanes, naphthalenes, and alkylbenzenes, along with several additives, including toluene and other solvents. A recent analysis of the same study population found that preovulatory luteinizing hormone levels were significantly lower in women whose total aliphatic hydrocarbon levels measured in exhaled breath were above the median.[4] Because organic solvents have been associated with various menstrual disorders, it is possible that they may affect vasomotor symptoms during menopause or could be responsible for causing menopause to occur years earlier in exposed workers. Although we did observe a modest increase in vasomotor symptoms in the highest exposure group, our sample of highly exposed workers was too small to adequately evaluate the effect.

Physical Symptoms

Unlike hot flashes or night sweats, the prevalence of urine leakage was not lower in the low-probability, low-intensity group of solvent-exposed women. The prevalence of vaginal dryness did not differ by exposure status. However, neither urine leakage nor vaginal dryness have been consistently associated with changing hormone levels during menopause,[34] and recent studies have not shown a strong relationship between these symptoms and hot flashes or night sweats.[32,35]

The lower prevalence of headache among both groups of women with low-intensity exposure to organic solvents was somewhat surprising. Previous studies of organic solvents used in the workplace such as trichloroethylene and methylene chloride have reported an increased prevalence of headaches in exposed workers.[9] In the Polish study of carbon disulfide, the prevalence of headaches was almost twice as high in the exposed women as in the control group.[3] However, a British study of headaches in civil servants found that a significantly larger proportion of executives, and clerical, typing, and data processing grades of staff reported headaches in the past 12 months compared with messengers, office keepers, and ushers.[44] As seen in Table 1, the managers, secretaries, and other clerical workers in this study were all in the nonexposed group. This may explain the lower frequency of headache in the low-intensity exposure group, which had few women with desk jobs. Too few women were included in jobs with high-intensity exposure to permit us to observe a significant elevation of headaches in the highest exposure group.

Psychologic Symptoms

Many studies of workers in a variety of industries have shown an association between impairment of memory and exposure to organic solvents.[8–14] Our finding of a twofold increased prevalence odds ratio for forgetfulness in the highest exposure group compared with working women with no exposure is consistent with those reports and warrants

TABLE 5
Adjusted Prevalence Odds Ratios (APORs) and 95% Confidence Intervals (CIs) for the Association Between Occupational Organic Solvent Exposure and Selected Symptoms in Middle-Aged Chinese and White Women

	Probability and Intensity of Occupational Exposure to Organic Solvents						
	None*	Low Intensity, Low Probability		Low Intensity, Medium or High Probability		Medium to High Intensity, Medium or High Probability	
Symptoms	APOR	APOR	95% CI	APOR	95% CI	APOR	95% CI
	(*N* = 717)	(*N* = 50)		(*N* = 41)		(*N* = 40)	
Hot flashes or night sweats†	1.00	0.48	0.19–1.21	0.69	0.29–1.62	1.27	0.56–2.88
Urine leakage‡	1.00	1.26	0.55–2.89	0.97	0.32–2.98	1.37	0.53–3.58
Vaginal dryness§	1.00	1.23	0.45–3.32	0.98	0.33–2.94	1.08	0.35–3.31
Difficulty sleeping‖	1.00	0.91	0.47–1.76	1.39	0.67–2.90	1.53	0.69–3.40
Stiffness/soreness¶	1.00	0.75	0.41–1.41	0.58	0.29–1.19	1.40	0.62–3.16
Headache#	1.00	0.51	0.27–0.98	0.40	0.18–0.87	0.76	0.36–1.60
Heart pounding**	1.00	0.54	0.19–1.58	0.88	0.32–2.38	0.93	0.32–2.66
Forgetfulness††	1.00	0.57	0.28–1.16	0.76	0.36–1.59	2.51	1.12–5.63
Tense/nervous‡‡	1.00	0.63	0.34–1.18	0.64	0.32–1.30	0.52	0.25–1.08
Depression§§	1.00	0.96	0.51–1.81	0.36	0.14–0.89	0.76	0.34–1.68
Irritability‖ ‖	1.00	0.78	0.43–1.42	0.87	0.43–1.73	1.44	0.66–3.17
General health¶¶							
Good or very good vs Excellent	1.00	0.44	0.22–0.89	1.37	0.47–4.00	1.26	0.34–4.64
Fair or poor vs excellent	1.00	0.68	0.10–4.60	0.59	0.06–5.44	2.02	0.22–18.21

*Referent category.
†Adjusted for education, menopausal status, ethnicity/language, and physical activity.
‡Adjusted for age, smoking, education, ethnicity/language, physical activity, and occupational status.
§Adjusted for age, menopausal status, ethnicity/language, and physical activity.
‖Adjusted for smoking, paying for basics, menopausal status, ethnicity/language, vasomotor symptoms, stiffness or soreness, depression, availability of help, and occupational status.
¶Adjusted for education, physical activity, history of arthritis, ethnicity/language, disability, availability of help, and occupational status.
#Adjusted for age, education, ethnicity/language, physical activity, and occupational status.
**Adjusted for smoking, education, menopausal status, ethnicity/language, parity, availability of help, and occupational status.
††Adjusted for age, education, menopausal status, ethnicity/language, physical activity, parity, disability, availability of help, and occupational status.
‡‡Adjusted for education, paying for basics, menopausal status, ethnicity/language, disability, availability of help, and occupational status.
§§Adjusted for age, education, paying for basics, ethnicity/language, physical activity, disability, and availability of help.
‖ ‖Adjusted for age, smoking, education, ethnicity/language, physical activity, parity, disability, availability of help, and occupational status.
¶¶Adjusted for smoking, education, paying for basics, menopausal status, ethnicity/language, physical activity, disability, availability of help, number of close friends, and occupational status.

further study in a larger group of highly exposed women.

The prevalence of reporting feeling sad or depressed was not elevated in the highest exposure group compared with the unexposed working women, consistent with the Polish study of carbon disulfide workers. In that study, 32.8% of exposed workers reported depression compared with 36.3% in the control group.[3] The lower prevalence in our group of women with low-intensity and medium–high probability of exposure to organic solvents compared with unexposed women (APOR = 0.36) is not explained by selection bias with respect to hormone use. The prevalence was low in both the HRT users and nonusers, and women in the low-intensity/medium–high-probability group were not more likely to take hormones than the women in the reference group. Perhaps the nature of the jobs in this group, which includes janitors and maids (Table 1), protects women from this symptom, although the finding could be the result of chance, because the number of women in this group is relatively small, and we made many comparisons in the analysis.

Strengths and Limitations

The present study had several strengths compared with previous work. Although several studies have been conducted to assess the effect of occupational organic solvent exposure on reproductive outcomes such as spontaneous abortion and menstrual cycle irregularities, this is the only U.S. study to date of which we are aware to examine the relationship between occupational organic solvent exposure and menopausal symptoms. Second, we were able to control for several important confounding variables not measured in the Polish study of menopausal symptoms and carbon disulfide exposure, including smoking, difficulty paying for basics, language, disability, availability of help and number of close friends (social support vari-

TABLE 6
Adjusted Prevalence Odds Ratios (APORs) and 95% Confidence Intervals (CIs) for the Association Between Probability and Intensity of Occupational Organic Solvent Exposure and Selected Symptoms in Middle-Aged Chinese and White Women

		Probability of Occupational Exposure to Organic Solvents				Intensity of Occupational Exposure to Organic Solvents			
	No Exposure*	Low Probability		Medium or High Probability		Low Intensity		Medium or High Intensity	
Symptom	APOR	APOR	95% CI	APOR	95% CI	APOR	95% CI	APOR	95% CI
	(*N* = 717)	(*N* = 53)		(*N* = 81)		(*N*= 91)		(*N* = 43)	
Hot flashes or night sweats†	1.00	0.53	0.23–1.25	0.96	0.53–1.75	0.59	0.32–1.12	1.27	0.59–2.74
Urine leakage‡	1.00	1.13	0.50–2.55	1.20	0.57–2.53	1.15	0.58–2.28	1.15	0.45–2.92
Vaginal dryness§	1.00	1.10	0.41–2.95	1.03	0.46–2.29	1.11	0.52–2.37	0.95	0.31–2.88
Difficulty sleeping‖	1.00	0.82	0.43–1.57	1.46	0.83–2.55	1.09	0.66–1.81	1.24	0.58–2.63
Stiffness/soreness¶	1.00	0.73	0.40–1.33	0.84	0.49–1.44	0.67	0.42–1.09	1.21	0.56–2.61
Headache#	1.00	0.51	0.27–0.95	0.55	0.32–0.95	0.46	0.28–0.77	0.73	0.35–1.49
Heart pounding**	1.00	0.49	0.17–1.40	0.90	0.43–1.91	0.69	0.33–1.44	0.78	0.28–2.18
Forgetfulness††	1.00	0.55	0.28–1.11	1.30	0.75–2.24	0.65	0.38–1.10	2.08	0.97–4.46
Tense/nervous‡‡	1.00	0.55	0.30–1.02	0.58	0.34–0.98	0.63	0.39–1.03	0.45	0.22–0.92
Depression§§	1.00	1.12	0.61–2.05	0.53	0.29–0.97	0.66	0.39–1.12	0.99	0.47–2.08
Irritability‖ ‖	1.00	0.81	0.45–1.45	1.08	0.63–1.84	0.82	0.51–1.30	1.43	0.67–3.04
General health¶¶									
Good or very good vs Excellent	1.00	0.46	0.23–0.92	1.34	0.58–3.10	0.64	0.35–1.17	1.32	0.36–4.81
Fair or poor vs excellent	1.00	1.26	0.26–6.02	1.07	0.22–5.20	0.65	0.14–2.97	3.13	0.43–22.93

*Referent category.
†Adjusted for education, menopausal status, ethnicity/language, and physical activity.
‡Adjusted for age, smoking, education, ethnicity/language, physical activity, and occupational status.
§Adjusted for age, menopausal status, ethnicity/language, and physical activity.
‖Adjusted for smoking, paying for basics, menopausal status, ethnicity/language, vasomotor symptoms, stiffness or soreness, depression, availability of help, and occupational status.
¶Adjusted for education, physical activity, history of arthritis, ethnicity/language, disability, availability of help, and occupational status.
#Adjusted for age, education, ethnicity/language, physical activity, and occupational status.
**Adjusted for smoking, education, menopausal status, ethnicity/language, parity, availability of help, and occupational status.
††Adjusted for age, education, menopausal status, ethnicity/language, physical activity, parity, disability, availability of help, and occupational status.
‡‡Adjusted for education, paying for basics, menopausal status, ethnicity/language, disability, availability of help, and occupational status.
§§Adjusted for age, education, paying for basics, ethnicity/language, physical activity, disability, and availability of help.
‖ ‖Adjusted for age, smoking, education, ethnicity/language, physical activity, parity, disability, availability of help, and occupational status.
¶¶Adjusted for smoking, education, paying for basics, menopausal status, ethnicity/language, physical activity, disability, availability of help, number of close friends, and occupational status.

ables), parity, BMI, and physical activity. However, we were not able to control for other potentially important variables such as diet, medications, and neurologic or psychologic history in the present analysis. Also, the measure of physical activity we had (self-reported physical activity compared with other women of the same age) was a global, and thus somewhat crude, measure. Both diet and physical activity will be examined in relation to symptoms subsequently in greater detail in the SWAN cohort. A third strength of the present study was that the participants were randomly selected from a health plan whose members are very representative of the population that it serves.[45] A study of the Kaiser Permanente Medical Care Program, Northern California Region showed that compared with the general population living in 22 counties in Northern California (including Alameda County, of which Oakland, Hayward, and Richmond are a part), Kaiser plan members have an approximately equal percentage of working class adults and adults with less than high school education as in the Census block groups were they live. However, somewhat more of the general population (13.2%) lived in blocks where more than 20% of adults lived below the poverty level than did Kaiser plan members (8.7%).

The present study also had some limitations. First, it was subject to all the limitations of a cross-sectional investigation. Thus, it was not possible to determine whether the occupational organic solvent exposure of a woman caused her to have certain symptoms or if having certain symptoms caused a woman to have a job with or without organic solvent exposure. For example, it is unknown whether women working in jobs with high organic solvent exposure become forgetful because of the exposure, or whether women who were forgetful could not hold other jobs

with less exposure, eg, those that require more mental work. We did, however, control for education and occupational status in this analysis. Second, we examined 11 symptoms and two general health assessments in three occupational groups for a total of 39 comparisons. By chance alone, two to three of these comparisons could be significant at the 0.05 level. Third, we assessed occupational exposure to organic solvents using a job-exposure matrix instead of actually measuring exposure for each woman. This method of exposure assessment inevitably leads to some misclassification of women. However, we did have a measure of probability of exposure, and restricting the women with medium and high intensity to those who also had medium and high probability may have lessened the misclassification. Additionally, we had too few women in the high-intensity group so that we had to combine them with the medium-intensity, thus possibly diluting the results. However, we have no reason to expect the misclassification to be nonrandom. Because we had more than two exposure categories, however, any bias created by the misclassification could drive our effect estimates either toward or away from the null.[46] Finally, our results may have been affected by selection bias with respect to hormone replacement therapy as described previously in this article.

Conclusions

This was the first population-based study to evaluate the relationship between occupational organic solvent exposure and symptom reporting in both white and Chinese midlife women. We found that occupational organic solvent exposure was strongly associated with a variety of important demographic and lifestyle factors, including ethnicity, smoking, education, physical activity, difficulty paying for basics, and occupational status. When we controlled for these important variables and menopausal status, organic solvent exposure was positively associated with forgetfulness and the perception of overall health as being fair or poor versus excellent. Although the sample size of women in the highest exposure group was small, and therefore our power to detect small differences was low, we did observe a somewhat increased prevalence of vasomotor symptoms, urine leakage, difficulty sleeping, stiffness, and irritability in this group of solvent-exposed women. These findings are important because they point out that a woman's occupational exposure to organic solvents may be related to symptoms and perception of overall health during the menopause transition. If these findings are confirmed in the longitudinal phase of the SWAN study, which has a larger sample size, further study of individual occupational cohorts of middle-aged women exposed to organic solvents may be warranted.

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